REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

Claims 1-7, 9-13 and 16-24 were pending. Claims 2 and 17 have been canceled without prejudice to future prosecution in a related application. Claim 25 has been added. Accordingly, claims 1, 3-7, 9-13, 16 and 18-25 are pending. Support for claim 25 may be found, for example, at page 5, lines 12-14.

Claims 1, 5, 16, 18-20 and 22 have been amended to focus on certain embodiments of the present invention, to clarify the claimed subject matter, or to enter minor edits. Such amendments have been made without prejudice to future prosecution of previously pending claims in a related application or acquiescence to the rejections in the Office Action. Support of the EDTA concentration recited in claims 1, 5, 16, 19 and 20 may be found, for example, at page 3, line 22. Support for the concentration of granulocyte macrophage colony-stimulating factor (GM-CSF) recited in claims 5 and 20 may be found, for example, at page 5, lines 12-14. The concentration of TRIS-HCl in mg/ml recited in claim 19 has been changed to the corresponding value in mM to be consistent with other claims. No new matter has been added via the claim amendments.

Rejections Under 35 U.S.C. 103(a)

Claims 1-7, 9 and 16-24 stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over the LEUKINE® Sargramostim product insert, in view of U.S. Patent No. 5,217,954 (Foster *et al.*) and U.S. Patent No. 6,620,784 (Ferrara *et al.*) and in the case of claims 4-8, further in view of U.S. Patent No. 5,545,536 (Kaushansky *et al.*) for reasons of record in the Office Action dated February 23, 2005. In addition, claims 10-13 stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over the LEUKINE® Sargramostim product insert, in view of U.S. Patent No. 6,620,784 (Ferrara *et al.*), U.S. Patent No. 5,217,954 (Foster *et al.*), and further in view of U.S. Patent No. 6,500,418 B1 (Dieckgraefe *et al.*) for reasons of record in the above-noted previous Office Action. In addition, it is asserted that the declaration by Dr. Scholz under 37 C.F.R. 1.132 filed June 27, 2006, is insufficient to overcome the above rejections because: (1)

the experiments described in the declaration do not compare the prior art composition with the claimed composition, (2) the results in the Declaration are not commensurate in scope with the claims; (3) the difference between the claimed composition and the prior art composition is minor at best and not a marked improvement.

Applicants respectfully traverse this ground of rejection. As indicated in the response filed August 18, 2005, Applicants believe that a *prima facie* case of obviousness has not been established. Further, even assuming *arguendo* that a *prima facie* showing has been made, Applicants respectfully submit that Dr. Scholz's Declaration previously submitted is sufficient to overcome the same. In addition, Applicants further submit a Declaration by Dr. Baumann under 37 C.F.R. 1.132 to support unexpected properties of the claimed composition. As discussed in detail below, these declarations establish that the double-peak absorption profile of GM-CSF after subcutaneous administration is unique to GM-CSF compositions that comprise EDTA, which enables not only an initial faster absorption of GM-CSF after subcutaneous injection, but also a subsequent sustained GM-CSF concentration in systemic circulation.

More specifically, as to the statement in the Office Action that the experiments described in Dr. Scholz's Declaration do not compare the prior art composition with the claimed composition, Applicants respectfully submit that it is unlikely that the differences between the compositions used in the experiments described in Dr. Scholz's Declaration and the prior art composition determine the presence or absence of the unique double-peak absorption profile of GM-CSF formulations. Applicants note that both the amounts of components in the "sargramostim EDTA" and the volume (*i.e.*, 1 ml) are given in the second paragraph of page 2 of Dr. Scholz's Declaration (*see,* line 3 of that paragraph for the volume). Accordingly, the concentration of sargramostim used in the experiments described in Dr. Scholz's Declaration is the same as in the prior art formulation. Regarding the difference in the manner how the protein has been stored and treated (lyophilized versus aqueous), Applicants submit that as indicated in Dr. Baumann's Declaration, it is unlikely that reconstitution of lyophilized sargramostim contributes to the lack of the double-peak absorption profile in the formulation that does not contain EDTA. Liquid formulation (3) in Dr. Baumann's Declaration (which does not contain EDTA), similar to the lyophilized sargramostim formulation (which also does not contain EDTA) described in Dr. Scholz's Declaration, did not show a double-peak absorption profile

(*see*, Exhibit 3 of Dr. Baumann's Declaration). Regarding the difference in the amount of benzyl alcohol, Applicants submit that also as indicated in Dr. Baumann's Declaration, it is unlikely that the minor difference in benzyl alcohol concentration contributes to the lack of the double-peak absorption profile in the formulation that does not contain EDTA. Neither of the two formulations in Dr. Baumann's Declaration that do not contain EDTA (*i.e.*, Formulations (2) and (3)) showed a double-peak absorption profile no matter whether the formulation contains Benzyl alcohol (*i.e.*, Formulation (2)) or not (*i.e.*, Formulation (3)).

As to the statement that the results in the Declaration are not commensurate in scope with the claims, while not acquiescing to the statement, to facilitate allowance, Applicants have amended the pending claims to recite the EDTA concentration to be 0.5 mM to 10 mM. Applicants note that although the concentration of EDTA in the formulation is indicated only in mg/ml in Dr. Scholz's Declaration, the corresponding concentration in mM (*i.e.*, 5.5 mM) is indicated in the response filed June 27, 2006 (*see*, the last line on page 5 of the response).

Applicants disagree with the statement in the Action that the difference between the claimed composition and the prior art composition is minor at best and not a marked improvement. Applicants submit that the double-peak absorption profile is unique to GM-CSF formulations that contain EDTA and provides unexpected advantages. More specifically, all the absorption profiles of GM-CSF formulations that contain EDTA in Dr. Scholz's and Dr. Baumann's Declarations are double-peaked (*see*, Exhibits 2-6 of Dr. Scholz's Declaration and Exhibits 2 and 3 of Dr. Baumann's Declaration), while all the profiles of GM-CSF formulation that do not contain EDTA are not (*see*, Exhibits 2, 3, and 6 of Dr. Scholz's Declaration and Exhibit 3 of Dr. Baumann's Declaration). In addition, the unique double-peak pharmacokinetic profile of the liquid formulation of sargramostim with EDTA after subcutaneous administration is unexpected and advantageous: It combines rapid initial absorption typically seen after intravenous administration of sargramostim formulations with subsequent slower absorption typically seen after subcutaneous administration of sargramostim formulations. The rapid initial absorption allows for sargramostim to be available earlier in systemic circulation and to elicit an earlier clinical benefit, whereas the following slower absorption phase allows for sustained sargramostim concentration in systemic circulation for a longer period of time post administration. Thus, the double-peak absorption profile combines the convenience and low cost

of subcutaneous administration with rapid absorption typically seen after intravenous administration.

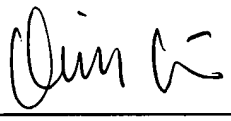
Accordingly, even assuming that a *prima facie* case has been made, Applicants respectfully submit that the unexpectedly advantageous properties for GM-CSF formulations with EDTA are sufficient to overcome the same, and request that this ground of rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Enclosures:
Declaration Under 37 CFR 1.132 with Exhibits 1-3

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